

I'm Denis Wirtz, Vice Provost for Research and professor of chemical and biomolecular engineering, materials science, pathology & oncology at Johns Hopkins University. AMA!

Denis<sub>Wirtz</sub><sup>1</sup>*andr/ScienceAMAs*<sup>1</sup>

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April 17, 2023

### Abstract

Hi Reddit! I am Denis Wirtz of Johns Hopkins University, where I wear two hats: Vice Provost for Research and T.H. Smoot Professor in the schools of engineering and medicine. I also direct the Johns Hopkins Physical Sciences-Oncology Center and co-direct the Cancer Nanotechnology Training Center, both funded by the National Cancer Institute, and serve as associate director of the Johns Hopkins Institute for NanoBioTechnology. As a faculty member, my lab conducts research in cancer: specifically, we are trying to determine the physical and biological underpinnings of metastatic disease, by far the primary cause of death in cancer patients. For example, my group was the first to establish how a 3-dimensional environment (think a 3D matrix) fundamentally affects the way cancer cells migrate, providing us with much more biologically and medically-relevant information than 2D studies (think Petri dishes) routinely used in the lab. Subsequent studies of the tumor microenvironment in simplified systems have increased our understanding of how cancer cells (we focus on pancreatic, breast, and ovarian cancer) migrate, morph, and are modulated by mechanical forces during metastasis. Our research has led me to re-evaluate what makes cancer lethal, often drug-resistant, and prone to recurrence after tumor removal. In the future, I am proposing a paradigm shift on how to diagnose tumors and develop new drugs, complementing the more mainstream genetic approaches. This is pertinent to US investments (biotech, big pharma, and federal agencies) in cancer treatments. In my other role as VP for Research, I work with my divisional colleagues to oversee all research at Johns Hopkins University, the largest recipient of federal funding in the US. In that capacity, I direct the Bloomberg Distinguished Professorships, the President's Frontier Award, research development, interdivisional research awards programs, improvements in research infrastructure, compliance and policies, etc. I have been particularly eager to help junior faculty (due to the current funding environment) and to promote collaborative, multidisciplinary research. I'm excited to speak with you about all things cancer and research! I will begin answering questions at 1 pm ET (10 am PT, 6 pm UTC). Ask me anything! Links: My lab: <http://wirtzlab.johnshopkins.edu/> VPR Profile: <http://web.jhu.edu/administration/provost/bios/wirtz> Faculty Profile: <http://engineering.jhu.edu/chembe/faculty/denis-wirtz/> Publications: [https://scholar.google.com/citations?user=UJP\\_JHEAAAAJ&hl=en](https://scholar.google.com/citations?user=UJP_JHEAAAAJ&hl=en) EDIT: I am signing off now. Thank you everyone for all your great questions. I look forward to doing this again.

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## Science AMA Series: I'm Denis Wirtz, Vice Provost for Research and professor of chemical and biomolecular engineering, materials science, pathology & oncology at Johns Hopkins University. I study the b

DENIS\_WIRTZ [R/SCIENCE](#)

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I'm excited to speak with you about all things cancer and research!

I will begin answering questions at 1 pm ET (10 am PT, 6 pm UTC). Ask me anything!

Links:

My lab: <http://wirtzlab.johnshopkins.edu/>

VPR Profile: <http://web.jhu.edu/administration/provost/bios/wirtz>

Faculty Profile: <http://engineering.jhu.edu/chembe/faculty/denis-wirtz/>

Publications: [https://scholar.google.com/citations?user=UJP\\_JHEAAAAJ&hl=en](https://scholar.google.com/citations?user=UJP_JHEAAAAJ&hl=en)

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I'm not entirely sure what to ask since I've never made it to an AMA like this while it was young. But here goes nothing.

CORRESPONDENCE:

Will there ever be a cure? Is that even possible? And why?

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This is the most important question one can ask about any disease, and in particular cancer. Great minds and phenomenal financial resources have been focused on cancer research, without finding a cure, at least for the big cancer killers, including lung cancer, prostate cancer, and breast cancer. Hence, it is safe to say one should think maybe less about a cure, and more about how to better manage the disease, i.e. how to keep the effects of the disease at bay, less about targeting the (multiple) origins and drivers of the disease.

What are examples of other current research projects that are most exciting at JHU? The highest recipient of federal research funds?! Must be because you deliver results. Cheers to you and your institution.

[cineblast](#)

There are so many good examples but I think what excites me the most is the range of projects that have arisen through collaboration across the institution. In the last year, the most widely followed JHU project was the Pluto Flyby by NASA's New Horizons. The JHU Applied Physics Laboratory was one of the two team leaders, responsible for mission management and development, and spacecraft integration and operations. The team included scientists from APL and our Krieger School of Arts & Sciences collaborating with NASA, SwRI, DOE, JPL, corporations and other universities. A few other examples: faculty from APL and the School of Medicine are coming together to engineer drones for the transport of blood samples in rural parts of sub-Saharan Africa. The Armstrong Institute for Patient Safety and Quality is taking major steps to reduce preventable errors in hospitals. Bloomberg Professor Chuck Bennett's team is on the final stages of building the CLASS Telescope to characterize the origin of the universe. These are all collaborations between JHU divisions and with scientists elsewhere. In grad school, you're told that you have to prove yourself on your own, and yet that's not usually how great advancements are made in research. This is not to say that students should not be deeply trained in a single topic. However, it's by bringing together experts from many fields that can help solve central problems facing the world. At Hopkins, oncologists are collaborating with engineers and physicists on developing new diagnostic and targeted therapies for cancer patients. Sociologists are working with epidemiologists and civil engineers to understand how climate change will affect people living in cities. While most prizes reward individuals (think the Nobel), it's never a scientist on an island (metaphorically) making a discovery. We need to change the way we publicly reward progress. Grants are currently awarding team science. Hence, public recognition should follow suit.

What's the most fascinating thing you found that you've come across through your research?

[warm20](#)

I think that would be our realization that human cells can feel the "dimensionality" of the space they live in, i.e. a flat surface versus a three-dimensional space. Over the years, we have learned much about how cells function (how cells divide, migrate, differentiate, etc.) using conventional flat dishes. These flat (Petri) dishes allow us to use powerful microscopes to visualize cells at high resolution. Some 6-7 years ago, my then PhD student, Stephanie Fraley, asked a simple question: do cells behave differently if fully embedded in a 3D matrix. Do cells migrate, divide, and differentiate essentially the same way in 3D as on flat (2D) surfaces? Long story short: absolutely not. What we have learned in 2D cannot predict – at all – how cells will behave in the more physiological environment of a 3D matrix. The same proteins may have completely different functions in cells placed on artificial dishes as opposed to cells in a 3D matrix. This is not to say that cells in the human body never live in 2D (cells that form the surface of organs live essentially in 2D). However, once set in motion, cells quickly encounter a 3D space. And, healthy cells don't migrate... they will move only in the context of disease

(cancer metastasis, immune response) and during embryonic development. We have since then observed that drug response of cancer cells is completely different in 3D from the 2D case. Quite a remarkable result, with major consequences in drug development and testing.

What do you look for in undergrads chosen to work/ assist in your lab? Do you generally prefer previous lab experience?

[slytherinyou](#)

I am a huge proponent of undergraduate research. This is a great way for students to find out if they like research at all, and also to learn in context sometimes esoteric material taught in the classroom. These days, getting an internship in industry or getting a job upon graduation effectively requires that undergraduate research experience. Our team is trying to beef up the ability of undergrads to find a host lab to do research. Many faculty would love to have undergrads in their lab, but don't know how to go about it, and vice versa, students would love to have more choices. At Hopkins, 40% say that that the number 1 reason they pick Hopkins over other universities is research opportunities.

As far as selecting a student for my lab, my own bias is choosing a student who is truly eager to do research, not looking for a resume-building activity. Past lab experience is not necessary and I've actually found no correlation between GPA and ability to highly achieve in the lab. I usually have between 15-20 undergrads working in my lab at a time and have found that success is often determined by a system of mentorship – post-docs mentoring grad students and grad students in turn being responsible for the development of undergrads. We try to create a strong cohort through shared events and experiences and a structured environment. I also require a commitment of at least two semesters. In the end, I'd say about 50% succeed in the lab – some realizing that research is indeed not their calling. Either way, it's great to be part of their process in figuring out where they want to focus their energy.

How do you balance running your lab with your administrative duties?

[paxprobellum](#)

I have to admit that I'm still working on figuring that out. Lots of coffee, that's for sure! I spoke on this topic recently with my departmental newsletter (see page 11): [http://engineering.jhu.edu/chembe/wp-content/uploads/sites/11/2015/10/JHU-ChemBE-Bond\\_9.15\\_19.pdf](http://engineering.jhu.edu/chembe/wp-content/uploads/sites/11/2015/10/JHU-ChemBE-Bond_9.15_19.pdf)

Hi, Dr. Wirtz! I'm a 2nd year PhD student at Hopkins in BME and also a part of INBT.

The current state of nanotechnology is relatively rudimentary despite much research since K. Eric Drexler's predictions back in 1986 in [Engines of Creation](#). We've certainly made progress, especially with greater computational resources to design things like DNA origami and molecular genome editing tools like CRISPR/Cas9, but do not seem to be on the verge of the breakthroughs that would allow us to create functional nanomachinery as capable as a bacterium, much less multi-enzyme complexes. *As associate director of INBT, do you foresee humanity making substantial progress in the realm of nanotechnology over the next 50 years?*

*As a side question, why do you think some many individuals in academia take a near pessimistic view of future technological progress?* I would consider Harvard's George Church an example of the opposite extreme bordering on over optimism of technological progress, but in my experience most professors are very hesitant to offer opinions on where humanity is headed as a whole.

Thanks!

[da6id](#)

.. that would allow us to create functional nanomachinery as capable as a bacterium Never say never...pace of development and discovery has been slow, for sure, but steady. A few years ago, there was clearly a sense we were on the verge of a breakthrough or even breakthroughs in nanotechnology for medicine...but as usual, especially when it's biomedical research, things take more time than anticipated. I am still confident - as long as funding keeps coming in - that we will be using smart nanoscale structures to address biomedical problems.

As a pharmacy student looking into going into hospital oncology. What advice would you give any healthcare professional going into the field of oncology

[SexySEAL](#)

Great question. Thanks. Here are some pieces of advice: (1) Expect the unexpected. The field of oncology is moving rapidly, both clinically and at the level of basic research that underlies these clinical treatments. Many predict that 50% of treatments may involve immunotherapy, treatments that are today still very experimental. Hence, what you learn in pharmacy school today, may be outdated soon. (2) Never forget whom you working for: the patient. Too many students, especially those involved in research, may too quickly forget that the end goal - the one that really counts - is to develop new diagnostic tools and improved, targeted treatments that don't degrade their health further.

There's a real problem in the academic world with overproduction of PhDs and a glut of faculty positions. It used to be that if you did this and this and this, then there was a position for you, but that's no longer the case. Still, the culture of overworking graduate students to the extreme is still very prevalent. And yeah, funding's bad but PIs are also staying way too long and milking their tenure past anything that's healthy for the system.

Do you ever foresee a systemic change where mandatory retirement ages are incorporated into American academics?

[waterwheel](#)

Maybe the issue is less about a glut of PhDs, and more about false expectations of what a PhD can do. Medicine and biomedical research are becoming more and more sophisticated and it still takes a PhD to understand, and meaningfully contribute to, modern medicine. But a PhD should not necessarily lead to one acceptable outcome: a faculty position in a research university, which was the old way to judge success. We have more and more students starting companies or joining established ones, and going to work for the federal government (DoD labs, Naval labs, NIH, NSF, DARPA, etc...). While there may be a higher ratio of graduating PhDs to available faculty positions, I think there are more "non-traditional" positions than ever before, and that's exciting. Relatedly, we have a program at JHU for retiring senior faculty, called The Academy, where they keep an office on campus and remain engaged in scholarly pursuits (<http://krieger.jhu.edu/theacademy/>).

Ok I actually have a good question this time around!

So as the VP for research, how do you combat publication bias in your research labs? Do you require every study to be published or registered? Additionally, how do you suggest that the scientific community as a whole, especially in sciences related to medicine, combat the problems associated

with publication bias?

[TheDocFeelGood](#)

Another great question! As scientists and engineers, we are supposedly trained to avoid bias. Yet, recent studies suggest that scientists are influenced by peers (group think), and by who funds their research (ex: tobacco companies, etc.) much more so than we would like to acknowledge. It only takes a few rotten apples or a few bad stories, to diminish the trust of citizens (read taxpayers), to change their perception of science, and turn science from a method to seek the truth, into a matter of opinion. That could mean the end of science, and therefore the end of medical progress etc. As a VP for research, I treat this very seriously. Therefore, I have asked key thought-leaders at Hopkins (for instance Arturo Casadevall) to develop a white paper which I hope will result in the organization of a major conference. Not only scientists, but also sociologists, philosophers, economists, historians of science, journal editors, etc. will help us develop new guidelines for how to do, review, and communicate results from scientific studies. We are at a crossroads, the way clinical trials were at a crossroads in the 70's and 80's. I prefer not to presume the outcome of this conference, but I will expect specific guidelines for moving forward.

In regards to Oncology, where do you expect to see the next major breakthrough in cancer treatments?

[PhysicsPhile](#)

Many exciting developments in immuno-therapy are coming down the pipeline.

What is navigating the research professor / administrator balance like? What's a typical day look like for you?

[robotmagician](#)

See response to paxprobellum above on the first part of your question. Typical day – two years on the job and there hasn't been one yet. It's a mix of meetings to coordinate research oversight across the university, move the Bloomberg Distinguished Professorship program continuously forward (we're hiring 50 of the top interdisciplinary faculty from around the world to JHU by 2018), organize and implement university-wide research awards programs such as the Catalyst and Discovery Awards, etc. I frequently meet with faculty, especially early career faculty, to find out how I can use my role to make their life easier. I quickly learned how different each field is in how they assess productivity. This also means there's rarely a one-size-fits-all approach to institutional research policy. I find these meetings the most useful as I really learn what policies or incentive programs to move forward or tailor.

How exciting is it in the world of oncology right now with all the recent advancements for treatments and even potential cures?

[Netflixandillpickles](#)

What is particularly exciting to me is that scientists and engineers with very different backgrounds want to contribute to the cancer fight and make a difference. It will take a village...

As a tissue engineering researcher, I would like to know what remaining advancements in 3D micro environments need to be made for commercialization? It seems the tumors on a chip promise to bring more accuracy yet have not been adopted in a widespread fashion.

[Pinkiezz](#)

Great field to be in. I think there is a huge untapped market for drug testing and alternatives to animal testing. So go for it!

I am proposing a paradigm shift on how to diagnose tumors and develop new drugs

What exactly do you mean by this? How do you seek to change cancer treatment?

[BlimpFruit](#)

Most current funding from the NIH's National Cancer Institute and private foundations is going towards identifying biomarkers and targeting gene mutations and epigenetic marks. Huge sequencing efforts are underway in the US and abroad (China, Europe). I am skeptical. This research is based on the flawed idea that genes are deterministic, i.e. once you know what the status of all genes is in a cell, you can determine its fate (whether it can form a tumor or metastasize, etc). I wish cancer were so simple. Anyone who has observed cells under a microscope will know the following: two daughter cells from the same single mother cell – which therefore have identical genetic backgrounds – will typically behave very differently: different shape, different size, different motility, different adhesion, etc. New research needs to acknowledge the genetic complexity of tumors and their functional complexity. When we track cells for a very long time (days, not hours), we observe dynamic changes in the cell phenotypes. A cell will dynamically switch from proliferative to motile, back to proliferative, all without any new stimulus. In other words, cancer cells have the intrinsic ability to form tumors (proliferative) and metastasize (migratory) and vice versa. Hence, developing drugs that specifically shrink tumors (the case of most cancer drugs) or target the metastatic cascade are not sufficient. Also, cells live in a complex microenvironment, with other cells that have been co-opted by cancer cells.

Hi Dr. Wirtz,

Do you think 3D cultures/scaffolds needs to become more common in research? As a current graduate student in a cancer lab, I've done mostly 2D cell culture. For example, do you see big differences in the EMT signature (or other characteristics) in 3D vs. 2D?

[ThirdRevelation89](#)

Yes, we do see major, qualitative differences in the way cells undergo EMT processes in 2D vs. 3D. It is now well-known that stiffness of the underlying matrix can trigger EMT. Hence, when you place cells on a 2D dish, you really do two things: they are in 2D AND they are exposed to a stiff environment. Unfortunately, you cannot extrapolate from your 2D results to predict what may happen in 3D. You have to bite the bullet and try out 3D matrices.

Is there an automated (3d printing like) mechanism that you use to create the 3d environment/scaffolding for your research?

Can tissue targeted delivery be achieved by incorporating ligands with liposomes?

Are there any novel methods for diagnosing or treating cancer that your teams are working on?

[Kevat](#)

We and others are working on making these 3D scaffolds in a more high-throughout manner. We used to make one gel at a time, we then moved to a multi-well system to look at 10-20 conditions at the

same time. We are now moving to hundreds of gels. Remember that in 2D, only ligand presentation and stiffness are the main parameters to think about. In 3D, you have to think about additional parameters, including local fiber alignment, pore size, etc. Bioengineers and materials scientists in the US and Europe are developing very clever ways to do control these parameters in 3D, independently. Not an easy task.

What's your view on the growing Anti-intellectualism that's seeping from public discourse and now into politics?

[yoohoofolife](#)

It is definitely growing and it is very alarming. Academics need to play their part by only publishing scientifically rigorous work. It just takes a few shaky papers to greatly damage the immense trust that the vast majority of American still has in science and scientists.

I have been recently researching nanotechnology in my high school biomedical class, and I was wondering how big and innovative you think nanotech will be in the cancer field, and how it might be applied?

[rccbtown](#)

We are still in the growth phase of the field. Nanotechnology for cancer has become mainstream in research. And now that some nanotech platforms are FDA approved, it is also becoming mainstream in the commercial arena.

As vice provost for research, you are responsible for overseeing research throughout the university, including social science and humanities departments. What are some examples of the great research going on at Hopkins in these realms?

[bio\\_artiste](#)

These were areas that I was really removed from in my time solely as a professor and an area I was quick to discover in my new role. I think the area of the digital humanities is burgeoning and we have some incredible research on the archaeology of reading being led by Earle Havens and Sayeed Choudhury (in collab with Princeton & UCL). You may have also heard about Bloomberg Distinguished Professor Kathy Edin's book "\$2.00 a Day: Living on Almost Nothing in America" (NYT best seller) on those living far below the poverty line in the US. Kathy is also the director of the 21st Century Cities Initiative, which brings together humanists, social scientists, policy experts, public health researchers, and more, to find solutions to urban issues. Pulitzer Prize winning composer Kevin Puts is working on a new symphony with his Johns Hopkins Discovery Award. And, just today, sociology professor Andrew Cherlin wrote up his research on rising death rates of white Americans:

[http://www.nytimes.com/2016/02/22/opinion/why-are-white-death-rates-rising.html?ref=opinion&\\_r=2](http://www.nytimes.com/2016/02/22/opinion/why-are-white-death-rates-rising.html?ref=opinion&_r=2) I could go on and on but I'm very excited about the work being done in these fields!

Do you see a way that Lung cancer could ever be cured without any risk in the future

[AroZi](#)

Lung cancer is by far the biggest killer for men and women. Little progress in treatment has been made since the war on cancer was declared by Richard Nixon. There is been quite a bit of progress in breast

and prostate cancer, but not nearly as much in lung cancer. Also too many people think that lung cancer is only caused by smoking and therefore, entirely preventable. This is cynical and I endorse more NCI funding going towards a cure for lung cancer.

Are you aware of the issue with synthetic phosphoethanolamine that's going on in Brazil? What is your opinion on the subject?

[bioscienceguy](#)

I am afraid, I don't know about this compound and possible effect on human health.

So far a lot of recent breakthroughs seem to focus on a specific cancer type (i.e. the fantastic T Cell therapy only studied acute lymphoblastic leukaemia so far), rather than covering a broad number. Obviously, cancer does have a lot of factors to consider, but do you believe that there could be a 'universal' cure for all cancers, or would we live in a world where pharmacies have a section filled with a drug for every type?

[pad-125](#)

Being a physicist by training and inclination, I come from a field that seeks universal laws. While there are many common traits among seemingly different cancers (for instance, all cancer cells have a ill-shaped nucleus, the central and common role that evolution plays in drug resistance, etc), I have to think that most likely we will have to find specific solutions for specific cancers, especially from a clinical point of view.